



# *Pharmaceutical Inspection Co-operation Scheme (PIC/S)*

Global Drug Development  
International Collaboration:  
Overview: PIC/S  
June 23, 23, 2014

Name: CARMELO ROSA, M.S., Psy.D.

Title: Director, Division International Drug Quality

Organisation: US FDA, CDER-OC, OMPQ

# Agenda

General Overview International Collaboration Initiatives

CDER-OC/OMPQ/DIDQ core functions related to our global interaction with international regulators

General Overview PIC/S

Conclusions

# Ongoing USFDA-DIDQ Pilots and Programs

## Active Pharmaceutical Ingredient (API) Program <sup>1</sup>

- ICH Q7 as common guidance for API inspections
- Scope limited to third country sites (sites not in the home jurisdiction of the participating agencies)
- Routine exchange of GMP inspection reports since 2009
- Joint Inspections conducted since 2009
- Regular monthly teleconferences since 2010
- Led to increased communication, transparency and established processes for further collaboration, including drug shortages, regulatory action notification, and drug application compliance decisions

## Precedent-setting Collaboration:

- In early 2012, FDA relied upon an EDQM inspection and subsequent Ph.Eur. Certificate suspension to take regulatory action (adding a firm to Import Alert 66-40); similar actions followed in 2012 and to present.



## Participants

FDA

European Medicines  
Agency (EMA)

European Directorate for  
the Quality of Medicines  
(EDQM)

Australia's Therapeutic  
Goods Administration  
(TGA)

Italian Medicines Agency  
(AIFA)

Irish Medicines Board (IMB)

UK Medicines and  
Healthcare Products  
Agency (MHRA)

Danish Medicines Agency  
(DKMA)

French Medicines Agency  
(ANSM)

World Health Organization  
(WHO)

<sup>1</sup> Reference Document: [API Program- Terms of Reference](#)

# Ongoing USFDA-DIDQ Pilots and Programs

## **Finished Dosage Pilot<sup>2</sup> and Mutual Reliance Pilot (FDA/EMA)<sup>3</sup>**

- “Sister” pilots to focus first on confidence building via joint GMP inspections of finished dosage manufacturing sites (Finished Dosage Pilot) and then moving to reliance upon inspection information provided (Mutual Reliance Pilot) for regulatory decision making
- Joint inspections of finished dosage manufacturing sites in each other’s territory only (US and EU) began in 2010
- Exchange of inspectional information in order to defer/waive inspections based on risk analysis began in 2011
- Goal is to build confidence in respective inspection programs to reduce FDA inspections in EU and reduce EMA/Member State inspections in the US, thereby enabling a shift in inspectional resources to other regions



<sup>2</sup> Reference Document: [FD Pilot- General Principles](#)

<sup>3</sup> Reference Document: [Mutual Reliance- General Principles](#)

# Ongoing USFDA-DIDQ Pilots and Programs

## Regulatory Cooperation Council GMP Pilot (FDA/Health Canada)<sup>4</sup>

- Part of larger White House Directive on US-Canada collaboration efforts in many industries – transportation, agriculture, environment, health and personal care products
- FDA's 3 initiatives:
  - Common Electronic submissions
  - Common OTC monographs
  - **Mutual reliance on routine GMP inspection reports**
- 18-month initiative to increase reliance on GMP inspection reports for risk-based firms of common interest in US and Canada
- Timeline: May 2012 – December 2013
  - Final public webinar held in May 2014
- Activities include sharing/comparison of inventory and observational inspections



<sup>4</sup> Reference Document: [RCC- White House Directive](#)

## FDA and PIC/S



Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S) mission: *"...to facilitate the networking between participating authorities and the maintenance of mutual confidence, the exchange of information and experience in the field of GMP and related areas, and the mutual training of GMP inspectors."*<sup>4</sup>

### FDA granted PIC/S membership in January 2012

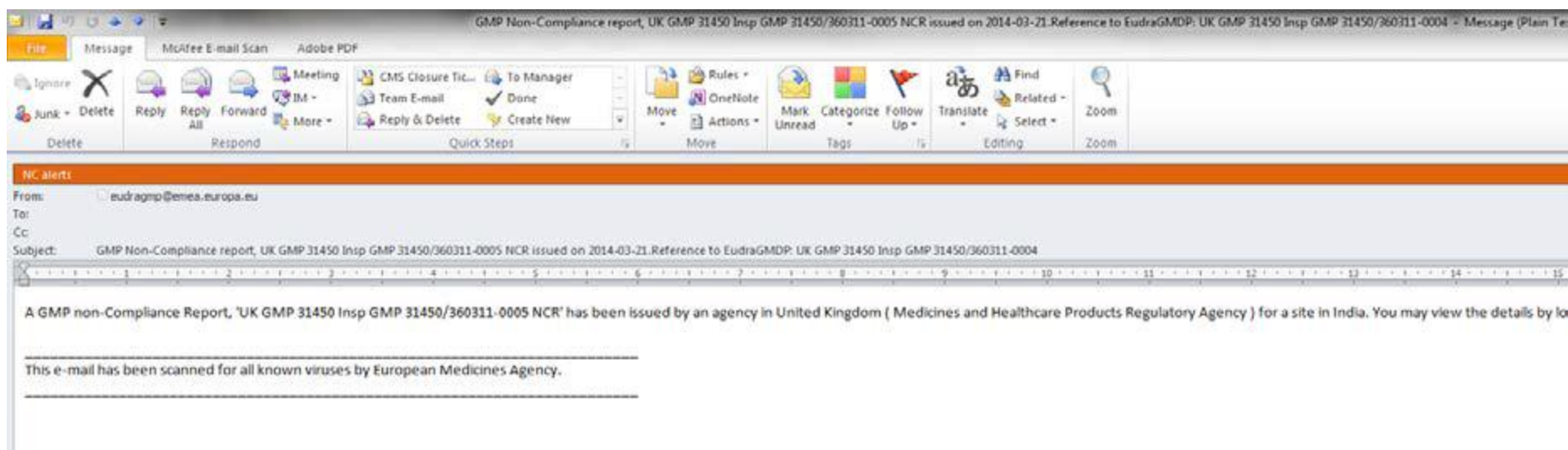
#### Current USFDA involvement with PIC/S Activities

- Prior knowledge and review of revisions to EU GMP regulations and PIC/S Guidances for industry
- Sharing of Inspection Planning with all PIC/S members
- Common Inspection Report Template to all PIC/S members
- Joint and Coached Inspection Training exercises
- Participation in "Expert Circle" groups, training, and discussions
- Co-chair of API Expert Circle, currently focusing on training opportunities in South Africa, Latin America, China and India

<sup>4</sup> PIC/S website: [www.picscheme.org](http://www.picscheme.org)

# Foreign Regulatory Authority Review in CMS

- Based on Non-Compliance Reports (NCRs) and alerts received from foreign regulatory agencies, inspection reports may be requested (generally top reason for request)







## EudraGMDP

English

### Welcome to EudraGMDP

EudraGMDP is the name for the Union database referred to in article 11(6) of Directive 2001/83/EC and article 80(6) of Directive 2001/82/EC. It contains the following information:

- Manufacturing and import authorisations
- Good Manufacturing Practice (GMP) certificates
- Statements of non-compliance with GMP
- GMP inspection planning in third countries

In addition the following new information is required in the database for the first time in 2013. As data transfer from national systems can be complex, it will take several months for all the National Competent Authorities to complete the uploading of this data

- Wholesale Distribution Authorisations
- Good Distribution Certificates (GDC)
- Statements of non-compliance with GDC
- Registration of manufacturers, importers and distributors of active substances for human use located in the EEA

Almost all information uploaded into the database is available to the general public. National Competent Authorities are able to exclude some information from public view. This includes information of a commercially sensitive or personal nature, inspection planning and information that may need to be restricted in the interests of security.

[Read-only access to EudraGMDP](#)

[Access to EudraGMDP application for registered users](#)

Users are advised that since inspections of manufacturers of active substances are based on risk, some active substance manufacturers may not be in possession of a GMP certificate issued by an EEA authority. The absence of a GMP certificate should not be understood as meaning that the active substance manufacturer in question does not comply with GMP.

EMA is not responsible for the contents of the database. Any questions on its content should be addressed to the relevant National Competent Authority.

The EudraGMDP database is maintained and operated by the EMA. Access to the general public is granted in order to enhance availability of information related to the EMA mandate. The content of the database is provided by the National Competent Authorities (NCA) of the EEA. For this reason, the EMA accepts no responsibility or liability whatsoever (including but not limited to) any direct or consequential loss or damage it might occur to you and/or any other third party) arising out of or in connection with the information on this database. Any questions about the content should be addressed to the relevant NCA. Please [click here](#) to get list of NCAs.

[EMA © 2007, EudraGMP 5.1.2.1 build 2014/03/14 17:31:28]



## EudraGMDP

MA | GMP | API REG | WDA | GDP | Sites

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Mon 24 Mar 2014 17:01:52 BST

### Welcome to EudraGMDP

Directives 2004/27/EC on human medicinal products and 2004/28/EC on veterinary medicinal products introduce the legal framework for the Community database.

The concept of a European Inspections database is included in the above specified legislation to provide EEA National Competent Authorities and the European Medicines Agency (EMA) with an overview of the status of pharmaceutical manufacturers. The legislation provides for an electronic tool containing complete information on all pharmaceutical manufacturers. This includes information on Manufacturing and Importation Authorisations (MA) and Good Manufacturing Practice (GMP) Certificates for authorised sites in the EEA and information on GMP certificates for manufacturers in third countries.



### Compliance with Good Manufacturing Practice:

A certificate of Good Manufacturing Practice (GMP) is issued to a manufacturer by the national competent authority that carried out an inspection if the outcome of the inspection confirms that the manufacturer complies with the principles of Good Manufacturing Practice, as provided by European Union legislation. If the outcome of the inspection is that the manufacturer does not comply a statement of non-compliance may be entered into EudraGMDP. Certificates and statements of non-compliance may be issued to manufacturers of medicinal products and manufacturers of active substances located inside and outside of the European Union.

[NCR Listing](#) to view recently submitted Non-Compliance Reports.

### Manufacturing and Importation Authorisation:

Manufacture of medicinal products in the EU or importation from a third country is subject to the holding of a Manufacturing and Importation Authorisation. The National Competent Authority of the Member State in which the manufacturer or importer operates issues these authorisations.

### Compliance with Good Distribution Practice:

A certificate of Good Distribution Practice (GDP) is issued to a wholesale distributor by the national competent authority that carried out an inspection if the outcome of the inspection confirms that the wholesale distributor complies with Good Distribution Practice, as provided by European Union legislation. If the outcome of the inspection is that the wholesale Distributor does not comply a statement of non-compliance may be entered into EudraGMDP. GDP certificates and statements of non-compliance may be issued to wholesale distributors of medicinal products and distributors of active substances.

### Wholesale Distribution Authorisation:

The wholesale distribution of medicinal products is subject to the holding of a Wholesale Distribution Authorisation. The National Competent Authority of the Member State in which the wholesale distributor operates issues these authorisations.

### Registration of Active Substance manufacturers, Importers and Distributors:

Manufacturers, importers and distributors of active substances are required to register their activities with the National Competent Authority of the Member State in which they operate.

The EudraGMDP database is maintained and operated by the EMA. Access to the general public is granted in order to enhance availability of information related to the EMA mandate. The content of the database is provided by the National Competent Authorities (NCA) of the EEA. For this reason, the EMA accepts no responsibility or liability whatsoever (including but not limited to any direct or consequential loss or damage it might incur to you and/or any other third party) arising out of or in connection with the information on this database. Any questions about the content should be addressed to the relevant NCA. Please [click here](#) to get list of NCAs.

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## EudraGMDP

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### GMP Compliance Menu

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[Non-Compliance Report](#)

[Withdrawn GMP Certificates](#)

### Non Compliance Reports

From Date: 2013-12-24 (YYYY-MM-DD) \*

To Date: 2014-03-24 (YYYY-MM-DD) \*

Include Withdrawn documents: ☐

Search

### GMP Non Compliance Search Results - 8 items

Report Number	Site Name	City	Country	Postcode	DUNS Number	EudraGMDP Key	NCA Ref	MIA Number	Issue Date	Status	Last Update By	Last Update Date
UK GMP 31450 Insp GMP 31450/360311- 0005 NCR	IND-SWIFT LIMITED	DISTRICT SAS NAGAR (MOHALI)	India	PIN-140507		8787	360311-IND-SWIFT LIMITED		2014-03-21		ngrewal (UK_MHRA)	2014-03-21 15:06:42 GMT
14MPP024	SOMET	MONACO	Monaco	98000		9170	A067 6922 697		2014-03-05		grenaud (FR_ANSM)	2014-03-10 12:54:23 GMT
13MPP057	Smruthi Organics Limited	Taluka Mohol	India	413 255 Solapur, Maharashtra		15103	151031360840861198		2014-01-08		sjellema (NL_IIGZ)	2014-02-28 09:45:25 GMT
sukis186744/2013	VAKOS XT a.s.	Přibram VI47	Czech Republic	261 01		3036	25656180_2	sukis53410/2013	2014-02-24		lvackavickova (CZ_SUKL)	2014-02-24 14:37:15 GMT
sukis186744/2013	VAKOS XT a.s.	Praha 8	Czech Republic	186 00		3035	25656180_1	sukis53410/2013	2014-02-24		lvackavickova (CZ_SUKL)	2014-02-24 14:28:00 GMT
IVS14-013/IV2	INDUSTRIAS GMB. S.A.	Castellbisbal	Spain	08755		23346	233461391590600821		2014-02-10		mtamo (ES_AEMPS)	2014-02-10 09:53:17 GMT
13MPP057	Smruthi Organics Limited	Taluka Mohol	India	413 255 Solapur, Maharashtra		15103	151031360840861198		2014-01-08		grenaud (FR_ANSM)	2014-01-15 12:11:24 GMT
13/13258-14	Suzhou No. 4 Pharmaceutical Factory	Suzhou	China	215 008		22767	227671389184259413		2013-12-06		bolsen (NO_NOMA)	2014-01-08 12:30:59 GMT



## EudraGMDP

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[Print Preview \(Short version\)](#)

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☐ Exclude Teleconference info

## Medicines and Healthcare Products Regulatory Agency

Report No : UK GMP 31450 Insp GMP 31450/360311-0005 NCR

### STATEMENT OF NON-COMPLIANCE WITH GMP

Exchange of information between National Competent Authorities (NCAs) of the EEA following the discovery of serious GMP non-compliance at a manufacturer <sup>(1)</sup>

#### Part 1

Issued following an inspection in accordance with :  
Art. 111(7) of Directive 2001/83/EC as amended

The competent authority of United Kingdom confirms the following:

The manufacturer : **IND-SWIFT LIMITED**

Site address : **OFF NH-21 VILLAGE JAWAHARPUR, TEHSIL DERA BASSI, DISTRICT SAS NAGAR (MOHALI), PUNJAB, PIN-140507, India**

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on **2013-10-23**, it is considered that **it does not comply with the Good Manufacturing Practice** requirements referred to in

- The principles and guidelines of Good Manufacturing Practice laid down in Directive 2003/94/EC <sup>(2)</sup>

<sup>(1)</sup> The statement of non-compliance referred to in paragraph 111(7) of Directive 2001/83/EC and 80(7) of Directive 2001/82/EC, as amended, shall also be required for imports coming from third countries into a Member State.

#### Part 2

Human Medicinal Products

**1 NON-COMPLIANT MANUFACTURING OPERATIONS**

**1.2 Non-sterile products**

**1 NON-COMPLIANT MANUFACTURING OPERATIONS****1.1 Sterile products**

*1.1.1 Aseptically prepared (processing operations for the following dosage forms)*

1.1.1.1 Large volume liquids

1.1.1.4 Small volume liquids

**1.2 Non-sterile products**

*1.2.1 Non-sterile products (processing operations for the following dosage forms)*

1.2.1.6 Liquids for internal use

**1.4 Other products or manufacturing activity**

*1.4.2 Sterilisation of active substance/ excipients/ finished product*

1.4.2.1 Filtration

**1.5 Packaging**

*1.5.1 Primary Packing*

1.5.1.1 Capsules, hard shell

1.5.1.13 Tablets

**Part 3**

**Nature of non-compliance :** 1. A critical deficiency was cited regarding potential product cross contamination, this deficiency was divided into two A. Potential chemical contamination, it was found that the company were manufacturing a potent cytotoxic (Amsacrine) product in the non-potent suite. Processes intended to contain the product had failed and cleaning process and verification were weak with contamination of general manufacturing seen. B. Potential microbial contamination. There were contaminated process media simulations that were not adequately investigated and root cause explained and mitigated. VHP sanitisation of the filling isolator inadequately controlled and validated and weaknesses in the environmental monitoring. 2. A major deficiency regarding the change control program (not all changes were controlled appropriately) and investigations, which were poor in quality regards to root cause analysis and corrective and preventative actions and were not performed in a timely manner. 3. A second major deficiency regarding maintenance of equipment and facilities with poor controls witnessed

**Action taken/proposed by the NCA :**

**Withdrawal, of current valid GMP certificate No. UK MIA 34140 Insp GMP/IMP 34140/113925-0006**

A restricted GMP certificate will be issued to permit continued manufacture and testing of products considered to be medically critical, as determined by the national competent authority.

# Foreign Regulatory Authority Review in CMS

- Once received, NCRs are input into CMS through a work activity #

MARCS-CMS > Work Add

Work Type: CDER - Foreign Regulatory Authority - Alert (NCR, suspensions, etc)		Officer 1: Tung, Lia (Division Project Manager)	
Team 1: CDER Division of International Drug Quality		Officer 2:	
Team 2:			

FEI # 3005895238 [View Details](#)

[Add](#) [Cancel](#)

# Foreign Regulatory Authority NCR Review in CMS

MARCS-CMS > [Last Search](#) / [Work](#)

**Record has been updated.**

Work # 74463 [History](#)

Work Type: CDER - Foreign Regulatory Authority - Alert (NCR, suspensions, etc) [?](#)

Work Status: In Progress [Converting into Case](#)

Accelerated Post Approval Recommendation: ☐ Yes

Joint Inspection: ☐ Yes

Date received: 03/21/2014 Create Date: 03/24/2014 Target Date: 04/11/2014 Close Date:

Foreign Agency: United Kingdom - Medicines and Healthcare Products Reg. Agency

Foreign Inspection Start Date: Foreign Inspection End Date: 10/23/2013

**Import Summary:**  
(Limit 4000 Characters)  
non-compliance with non-sterile products, packaging, quality control testing. could not confirm validity of stability testing data. falsified and inaccurate results reported in long term stability and batch testing. discrepancies in process validation and release data. failure to disclose data integrity issues for all products.

Inspection history?: Yes [?](#)

Named in FDA applications?: Yes [?](#)

FDA action taken: Requested report [?](#)

**Reason for Decision/Action:**  
(Limit 4000 Characters)  
enough evidence that products imported to the U.S. market from firm could be of concern. will request report from MHRA.

Firm: FEI # 300589523 Firm Name: Ind-Swift Laboratories Limited Country: India

**Center**  
Center Name: CDER

Team 1: CDER Division of International Drug Quality Officer 1: Tung, Lisa (Division Project Manager)

Team 2: Officer 2:

[Update](#) [Cancel](#)

[Documents \(0\)](#) [Activity Notes \(0\)](#) [Tasks \(0\)](#) [Linked WA \(0\)](#)

[Recommendation \(0\)](#) [Evidence \(0\)](#) [Final Outcome \(0\)](#) [PA Evidence \(0\)](#) [CIM \(0\)](#) [POST Inspection \(0\)](#) [POST Action Mgt \(0\)](#) [Complaint \(0\)](#) [Email \(0\)](#) [Add](#)

An organization's reference documents that are required to move a recommended action through the process.

[IHHE \(0\)](#) [Memoranda \(0\)](#) [ORA \(0\)](#) [Center \(0\)](#)

No files





# Foreign Regulatory Authority Review in CMS

- Request is sent to Foreign Regulator

Follow up.

No Categories (colored by Outlook 2003 Orange flag)

From: ☐ CDER International GMP  
To: ☐ CDER EXSEC  
Cc: ☐ CDER International GMP; ☐ Molzon, Justina A; ☐ Arellano, Shena; ☒ OC-OIP-Europe; ☐ Cruz, Concepcion; ☐ Rosa, Carmelo R; ☐ Soreth, Janice M  
Subject: Foreign Agency Report Request: Micro Labs Limited (IN)

Sent: Mon 5/20/2013 9:21 PM

CDER would like to request the April 22-26, 2013 inspection report, if available, from MHRA for the firm indicated below.

Micro Labs Limited  
Plot No. 113-116 4th Phase KIADB  
Bommasandra Industrial Area, Anekal Taluk  
Bangalore, IN  
FEI #3009310198

Thank you,

Lisa Tung  
CDER Office of Compliance  
Office of Manufacturing and Product Quality  
Division of International Drug Quality  
International Compliance Branch



# Foreign Regulatory Authority Review in CMS

- Foreign Regulator sends back report if available

Follow up.

No Categories (colored by Outlook 2003 Orange flag)

From: inspectionplanning, <inspectionplanning@mhra.gsi.gov.uk>

Sent: Wed 7/3/2013 3:54 PM

To: Arellano, Shena

Cc: Molzon, Justina A; OC-OIP-Europe; Cruz, Concepcion; Rosa, Carmelo R; Soreth, Janice M; Farbman, Mary; CDER EXSEC; CDER International GMP

Subject: RE: Urgent Foreign Agency Report Request: Eisai Limited (UK)

Message GMPReportEisai.pdf (92 KB)

THE INFORMATION CONTAINED IN THIS EMAIL IS SHARED WITH YOU UNDER THE TERMS OF OUR CONFIDENTIALITY ARRANGEMENTS

Dear Shena

Please find the report attached.

Kind regards,  
Jo

Joanna Milborrow  
Inspection Services Executive  
MHRA  
151 Park Street, Bristol, England, BS1 2NE, UK

Safeguarding public health



## **INSPECTION REPORT**

**Eisai Manufacturing Ltd.**  
European Knowledge Centre,  
Mosquito Way,  
Hatfield  
AL10 9SN

**Sentinel Case Folder:**  
**Insp GMP/GDP/IMP 32301/726219-0004**

# Foreign Regulatory Authority Review in CMS

- DIDQ management will assign work activity to a Compliance Officer/Consumer Safety Officer for review
- Some information will be pre-filled upon assignment, the rest is for your review
- Ensure all dates, Foreign Agency, 'triaging info', application information (if applicable) outcome, GMP problems, documents, activity notes are completed
- Ensure that the Foreign Reg Report Assessment Tool is filled out in Excel and uploaded to each Work Activity

# Foreign Regulatory Authority Review in CMS

- Once received, FRARs are input into CMS

MARCS-CMS » **Work Add**

Work Type: CDER - Evaluate Foreign Reg. Authority Report ⓘ

Team 1: CDER Division of International Drug Quality ▼

Officer 1: Tung, Lisa (Division Project Manager) ▼

Team 2:  ▼

Officer 2:  ▼

FEI #  Firm Finder

Add

Cancel

# Foreign Reg Report Review – Part 1

http://cms.fda.gov/vts/work/default.cfm?page=work&workid=76187

File Edit View Favorites Tools Help

X Convert Select

Page Safety Tools

MARCS-CMS >> [Last Search](#) / [Work](#)

**Work # 76187** [History](#) **Work Type:** CDER - Evaluate Foreign Reg. Authority Report **Work Status:** In Progress [Converting into Case](#)

**Date Complete EIR Received:**  **Create Date:** 06/06/2014 **Target Date:** 07/24/2014 **Close Date:**

**Date RAI Sent:**  **Date RAI Response Received:**

**Foreign Agency Outcome:**  **Action Taken From Review:**

**Foreign Agency:** Canada - Health Canada

**Foreign Inspection Start Date:** 04/29/2014 **Foreign Inspection End Date:** 05/09/2014

**Reason for report request:** Surveillance/general use

**Firm registered with FDA?:**

**Firm actively shipping to the US?:**

**Firm** **FEI # 3002316185** **Firm Name:** Shandex **Country:** Canada

**Application Data**

Type	Number	Supplement	User Fee Date	Status
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

Add

# PIC/S Overview

- ❑ History of PIC/S and PIC
- ❑ Role & Functions of PIC/S
- ❑ PIC/S Accession Procedure
- ❑ PIC/S Guides & Recommendations
- ❑ PIC/S Seminars & Expert Circles
- ❑ PIC/S Quality Systems

# History



PIC	Pharmaceutical Inspection Convention
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PIC Scheme	Pharmaceutical Inspection Cooperation Scheme
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Both operate in parallel under the logo/abbreviation



# History

## **PIC = Pharmaceutical Inspection Convention**

- Founded by The European Free Trade Association (EFTA) in October 1970
- PIC is a legal Treaty between countries
- Initially only 10 member countries:  
Austria, Denmark, Finland, Iceland,  
Liechtenstein, Norway, Portugal, Sweden,  
Switzerland and UK.

# Original Goals

- ✓ Harmonised GMP requirements
- ✓ Mutual recognition of inspections
- ✓ Uniform inspection systems
- ✓ Training of Inspectors
- ✓ Mutual confidence

# PIC membership as at January 1995

## Pharmaceutical Inspection Convention

(a Treaty between countries below)

18 Member countries:

*Australia, Austria, Belgium, Denmark, Finland,  
France, Germany, Hungary, Iceland, Ireland,  
Italy, Liechtenstein, Norway, Portugal, Romania,  
Sweden, Switzerland, United Kingdom.*

# Reason for creating the PIC Scheme

- After 1993, no new members of PIC possible
- Reasons:
  - Under EU law, only European Commission authorised to sign agreements with other countries
  - Expansion of PIC not possible unless European Commission became a member of PIC
  - Amendment of Convention difficult & lengthy
  - Inspectorates (& industry) favoured maintaining the principles of PIC
- Consequently, the PIC Scheme was developed & implemented.

# Main features of PIC Scheme

- Commenced operating on 2 Nov. 1995
- An informal arrangement between Agencies
- Networking and confidence building
- Exchange of information and experience on GMP
- Development of Quality Systems for Inspectorates
- Training of inspectors
- International harmonisation of GMP
- No obligation to accept inspection reports
- PIC & PIC/S operate in parallel - jointly referred to as **“PIC/S”**

# PIC/S Goal

“To lead the international development, implementation and maintenance of harmonised GMP standards and quality systems of inspectorates in the field of medicinal products”.

# Achievement of PIC/S Goal

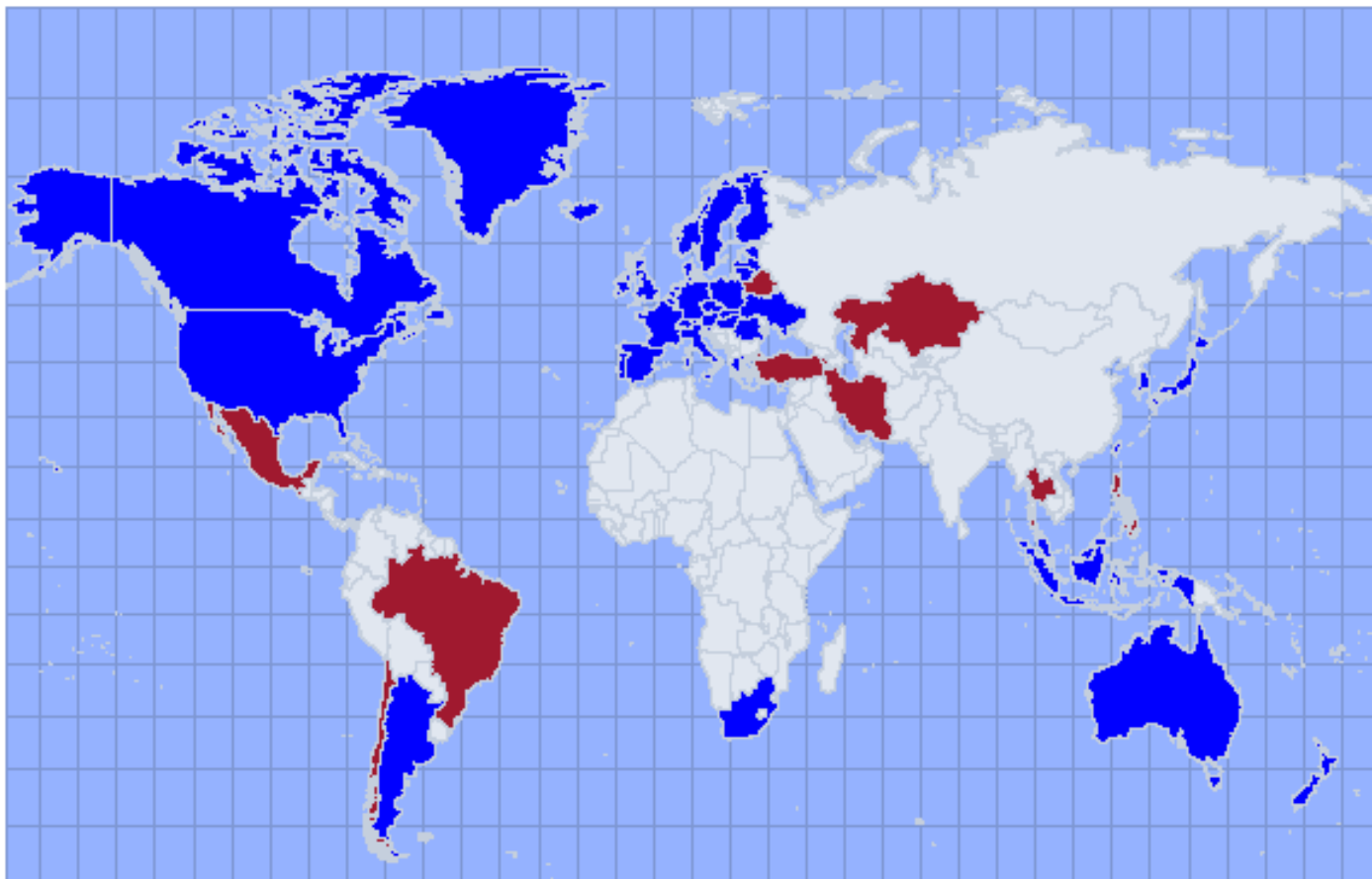
PIC/S Goal to be achieved by:

- ✓ Developing and promoting harmonised GMP standards and guidance documents.
- ✓ Training competent authorities, in particular GMP inspectors.
- ✓ Assessing (and reassessing) GMP Inspectorates.
- ✓ Facilitating the co-operation and networking for competent authorities and international organisations.

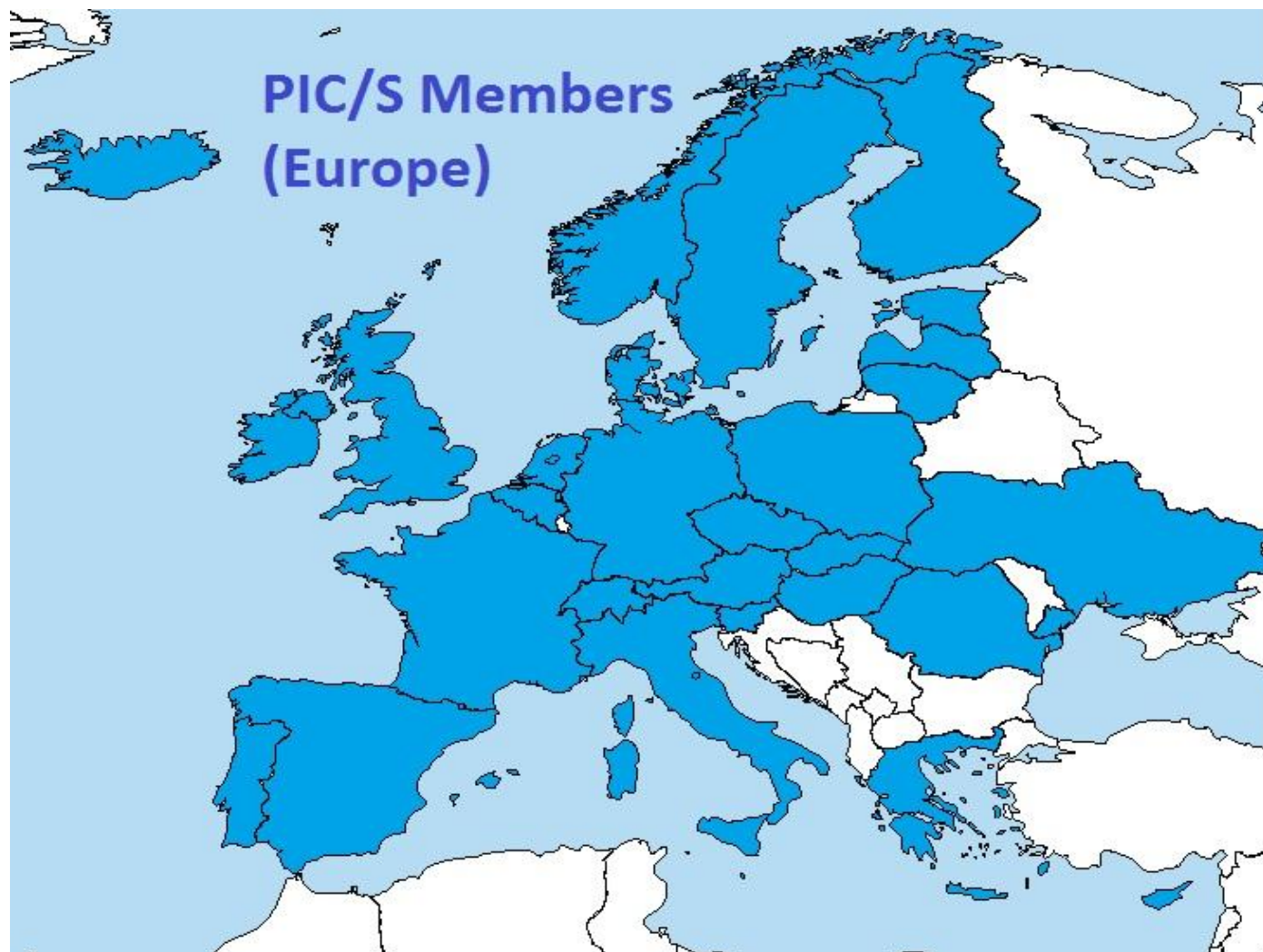


# 46 PIC/S Members (as of 1 July 2014)

## 10 PIC/S Applicants & Pre-Applicants



# PIC/S Members (Europe)



AUSTRIA  
 BELGIUM  
 CZECH REP. (Human & Vet)  
 CYPRUS  
 DENMARK  
 ESTONIA  
 FINLAND  
 FRANCE (Human & Vet)  
 GERMANY  
 GREECE  
 HUNGARY  
 ICELAND  
 IRELAND  
 ITALY  
 LATVIA  
 LIECHTENSTEIN  
 LITHUANIA  
 MALTA  
 NETHERLANDS  
 NORWAY  
 POLAND  
 PORTUGAL  
 ROMANIA  
 SLOVAK REPUBLIC  
 SLOVENIA  
 SPAIN  
 SWEDEN  
 SWITZERLAND  
 UKRAINE  
 UNITED KINGDOM (Human & Vet)

# PIC versus PIC/S

## PIC

- ☐ Convention
- ☐ Between countries
- ☐ A formal treaty
- ☐ Has legal status
- ☐ Focus on inspection
- ☐ Mutual recognition of inspections

## PIC/S

- ☐ Scheme
- ☐ Between agencies
- ☐ An informal arrangement
- ☐ Has no legal status
- ☐ Focus on training & Developing guidelines
- ☐ Exchange of information

## Benefits of PIC/S Membership

- ✓ Accession forced improvements – i.e. discipline
- ✓ Cost saving – import control mechanism
- ✓ Facilitated exports of medicines
- ✓ Training (seminars, Joint Inspections, etc.)
- ✓ Involvement with developing international GMPs
- ✓ Facilitated MRA with EC
- ✓ Networking & personal contacts

## How PIC/S operates

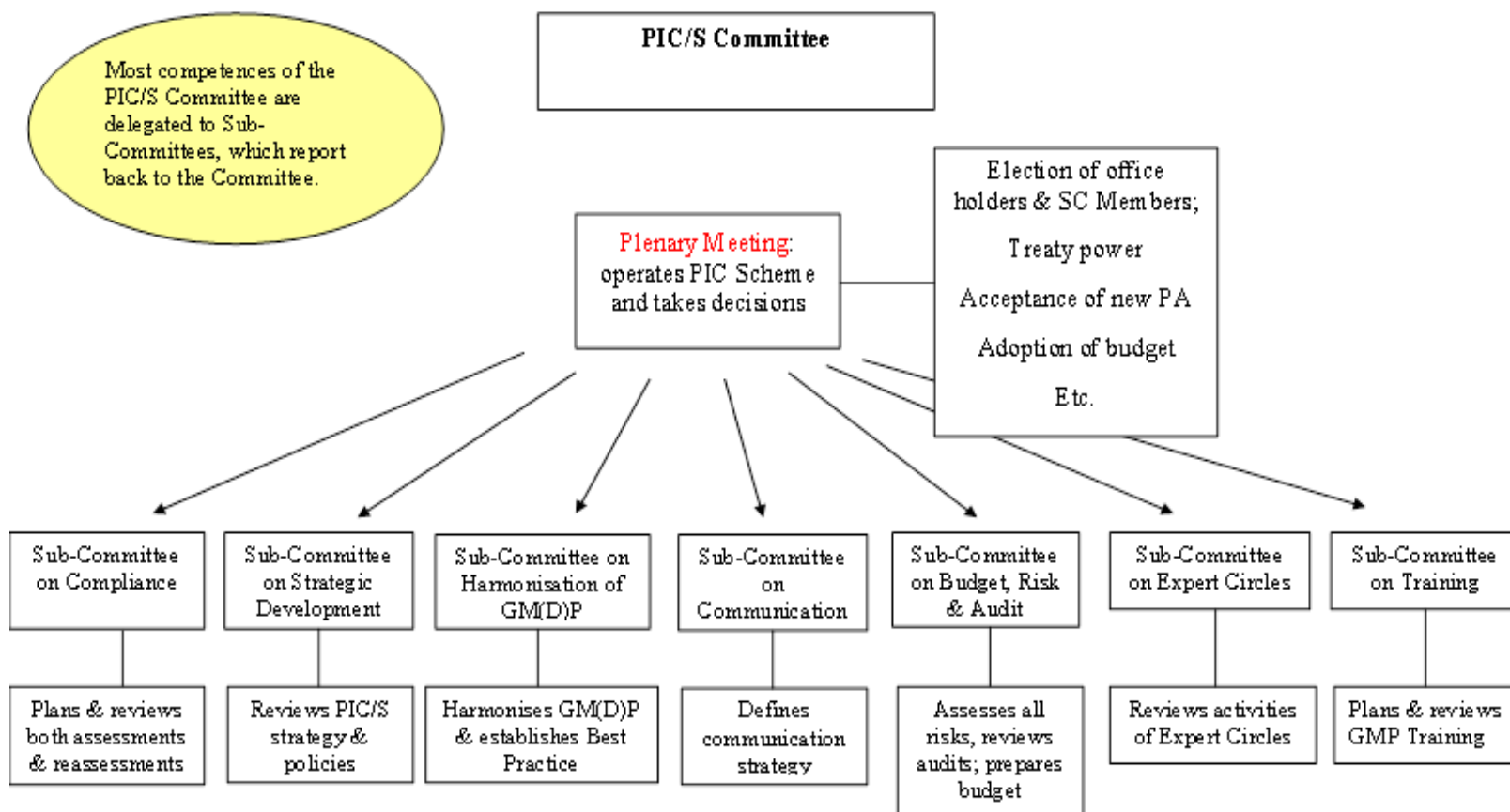
- PIC/S Committee
- Secretariat
- Executive Bureau: Chair, Deputy Chair, past Chair, seven Chairs of Sub-Committees
- Small Budget
- Good relationship and co-operation
- Training opportunities
- Exchange of information, rapid alerts
- Development of GMP guidelines

# New PIC/S Organisational Sub-Committee Structure

To reply to PIC/S's growing membership, a new Sub-Committee structure has been developed and come in force 1<sup>st</sup> January 2014, in order to:

- Favour the participation of all PIC/S Participating Authorities
- Establish a more participative and efficient organisation of PIC/S, where each Sub-Committee will be responsible for its respective core areas and will take the lead in developing policies.

# PIC/S new structure as of 1 January 2014







## Accession dates (1)

### Accession to PIC

### Accession to PIC/S

Austria	May 1971	Nov 1999
Denmark	May 1971	Nov 1995
Finland	May 1971	Jan 1996
Iceland	May 1971	Nov 1995
Liechtenstein	May 1971	Nov 1995
Norway	May 1971	Nov 1995
Portugal	May 1971	Jan 1999
Sweden	May 1971	Feb 1996
Switzerland	May 1971	Feb 1996
UK	May 1971	Jun 1999
Hungary	Aug 1976	Dec 1995
Ireland	Dec 1977	Feb 1996
Romania	May 1982	Nov 1995
Germany	Sep 1983	Dec 2000
Italy	Aug 1990	Feb 2000
Belgium	Sep 1991	Feb 1997
France	Dec 1992	Feb 1997
Australia	Jan 1993	Nov 1995
Netherlands	-	Nov 1995

## Accessions dates (2)

### Accession to PIC

### Accession to PIC/S

Spain	-	Jan 1998
Canada	-	Jan 1999
Singapore	-	Jan 2000
Greece	-	Jan 2002
Malaysia	-	Jan 2002
Latvia	-	Jan 2003
Czech Rep (Vet)	-	Jul 2005
Poland	-	Jan 2006
Estonia	-	Jan 2007
South Africa	-	Jul 2007
Argentina	-	Jan 2008
Malta	-	Jan 2008
Cyprus	-	Jul 2008
France (Vet)	-	Jan 2009
Israel	-	Jan 2009
Lithuania	-	Jul 2009
USA	-	Jan 2011
Ukraine	-	Jan 2011
Slovenia	-	Jan 2012
Indonesia	-	Jul 2012



## Accessions dates (3)

### Accession to PIC

**New Zealand**

**Chinese Taipei**

**United Kingdom (Vet)**

**Japan -**

**Korea (Republic of)**

### Accession to PIC/S

**-Jan 2013**

**-Jan 2013**

**-Jan 2014**

**-Jul 2014**

**-Jul 2014**

## Applicants being assessed for membership

- Brazil / ANVISA
- Hong-Kong SAR / PPBHK
- Iran / MoH
- Philippines / PFDA
- Thailand / Thai FDA
- Turkey / TMMDA

## Applicants for Pre-Accession

- Armenia / SCDMTE
- Belarus / MoH
- Chile / ISP
- Kazakhstan / CCMPA
- Mexico / COFEPRIS

## Agencies showing interest in joining PIC/S

- China / CFDA
- Croatia / HALMED
- Nigeria / NAFDAC
- Russia / Roszdravnadzor
- Saudi Arabia / SFDA
- Thailand / Thai FDA
- Zimbabwe / MCAZ

# Accession+ Pre-accession procedure

## Useful Documents

- Pharmaceutical Inspection Cooperation Scheme (PIC/S 1/95)
- Guidelines for Accession to PIC/S (PS/W 14/2011)
- Questionnaire for Competent Authorities (PS/W 1/2011)
- Audit Checklist (PS/W 1/2005)
- Recommendations on quality system requirements for pharmaceutical inspectorates (PI 002)

# 1. Pre-accession procedure

- As some of the new applicants may have notable differences or are not familiar to PIC/S standards, a new “period” offers a “softer” approach and more time to adjust.
- It is a kind of pre-assessment and gap analysis of the Applicant Authority to the PIC/S requirements and a possible on site visit of an “auditor” appointed by the Committee
- Time frame up to 2 years
- Then, time to decide for the application. Is the Applicant ready?  
The Committee will decide on the next steps (invitation to apply or further delay to prepare)



## 2. Accession procedure

### *Steps to Accession*

- General interest & commitment, eg. attend Seminars
- Written application to Secretary + supporting documents
- PIC/S Committee appoints Rapporteur to evaluate
- Applicant invited to Committee meeting to answer questions of Rapporteur and Committee
- PIC/S delegation undertakes assessment visit (Inspectorate's procedures; observe 3 or 4 inspections)
- Delegation report issued (to applicant & Committee)
- Committee decides on membership.

# PIC/S GMP Guide

## Virtually identical to EC GMP Guide

(main difference = "Qualified Person" vs. "authorised person")

## Basic GMP Guide (Part I)

## GMP Guide for APIs (Part II)

## Plus Annexes, covering:

- Sterile Medicinal Products
- Sampling of Starting Materials & Packaging Materials
- Pressurised Metered Dose Aerosols
- Liquids, Creams & Ointments
- Computerised Systems
- Radiopharmaceuticals

# PIC/S GMP Guide (2)

## Plus Annexes, covering:

- Biologicals
- Herbals
- Medicinal gases
- Use of Ionising Radiation
- Investigational Medicinal Products
- Products Derived from Human Blood & Plasma
- Qualification and Validation
- Parametric release
- Reference and Retention Samples

# Development of GMP Guidance Documents

- Usually initiated at end of PIC/S Seminars
- PIC/S Working Group formed
- Author prepares draft
- Comments from Working Group
- Comments from PIC/S Inspectorates
- Comments from Industry
- Endorsed by PIC/S Committee for general distribution
- Simultaneous distribution by EMA (& vice versa)

# PIC/S Works on Validation

- 1994 PIC Seminar in Ireland on Validation identified need to develop guidance document
- PIC/S Recommendations prepared covering:
  - Validation Master Plan
  - Installation & Operational Qualification (IQ & OQ)
  - Non-sterile Process Validation
  - Cleaning Validation
- PIC/S entry into force on 1<sup>st</sup> March 1999
- Adopted by the EU as Annex 15 to EU GMP Guide

# Some PIC/S Recommendation & Guideline Documents

- ✓ PIC/S GMP Guide (similar to EU GMP Guide).
- ✓ PIC/S GMP Guide for Blood Establishments.
- ✓ PIC/S Guide to Good Practices for the Preparation of Medicinal Products in Healthcare Establishments.
- ✓ Validation (master plan, IQ/OQ, process, cleaning).
- ✓ Validation of Aseptic Processes.
- ✓ Inspection of Isolator Technology.
- ✓ Quality Systems for Inspectorates.
- ✓ Sterility Testing.
- ✓ Validation of Computerised Systems.

# PIC/S Involvement in the ICH GMP Guide on APIs

- PIC/S Conference in Canberra 1996:
  - consensus obtained to prepare international GMP.
- PIC/S draft document prepared during '97 & '98.
- ICH Q7 took over the work of PIC/S mid-1998 to enable industry to become involved:
  - ICH involves 3 regions (USA, Europe & Japan).
- ICH GMP Guide finalised in November 2000 after extensive public consultation.
- Most countries have adopted ICH document as a GMP requirement for APIs by 1<sup>st</sup> April 2001 (EU).
- ICH document became Part II of PIC/S GMP Guide in 2007

# PIC/S Seminars (1)

- |   |                   |
|---|-------------------|
| - Packaging & Labelling                       | Switzerland, 1971 |
| - Contamination                               | Sweden, 1972      |
| - Quality                                     | France, 1972      |
| - Sampling & Analytical Control               | UK, 1973          |
| - Contract Manufacture & QC                   | Switzerland, 1974 |
| - QC Department                               | Denmark, 1975     |
| - Stability                                   | Austria, 1976     |
| - Isolation/ID/Quantification of Drugs        | Sweden, 1977      |
| - Tablet Manufacture                          | UK, 1978          |
| - Large Volume Parenterals                    | Norway, 1978      |
| - PIC Basic GMP Guide<br>(Need for Revision?) | Finland, 1979     |
| - Tablet Manufacture                          | Denmark, 1980     |
| - Manufacture of Active Ingredients           | Switzerland, 1980 |



## PIC/S Seminars (2)

- |  |                   |
|--|-------------------|
| - Control Laboratory                                   | Hungary, 1981     |
| - Validation   | Ireland, 1982     |
| - Packaging  | Portugal, 1983    |
| - Production of Biological Products                    | Germany, 1984     |
| - Premises   | Norway, 1985      |
| - Plastics   | Sweden, 1986      |
| - Inspection   | UK, 1987          |
| - Water  | Switzerland, 1988 |
| - Contamination Risk in the Manufacture of Parenterals | Austria, 1989     |
| - Blood & Blood Products                               | Denmark, 1990     |
| - Audit - Pharmaceutical Inspection                    | Hungary, 1991     |
| - Products Derived from Biotechnology                  | Italy, 1992       |

# PIC/S Seminars (3)

- Inspection & Testing in Relation to the Marketing Authorisation
- Qualification & Validation
- Manufacture of Sterile Products
- Computer Systems
- GMP Standards for APIs
- Manufacture & Inspection of APIs
- Quality Systems for Inspectorates
- Non-technical Aspects of Inspection
- Biotechnology
- Inspection of Utilities
- Interface between GCP and GMP

Belgium, 1993  
Ireland, 1994  
Iceland, 1995  
Australia, 1996  
Australia, 1996  
Finland, 1997  
Holland, 1998  
UK, 1999  
France, 2000  
Czech Rep, 2001  
Canada, 2002

# PIC/S Seminars (4)

- |   |                    |
|---|--------------------|
| - Inspection of QC laboratories                         | Slovak Rep, 2003   |
| - Inspection of APIs                                    | Spain, 2004        |
| - Primary packaging, labelling and prevention of mix-up | Romania, 2005      |
| - Risk Management                                       | Germany, 2006      |
| - Solid Dosage Form Manufacturers                       | Singapore, 2007    |
| - Good Distribution Practices                           | Poland, 2008       |
| - Sterile Aseptic Manufacturing                         | Sweden, 2009       |
| <br>  |                    |
| - Herbal / Traditional Medicines                        | Malaysia, 2010     |
| - Good Inspection Practices                             | South Africa, 2011 |
| - Qualification and Validation                          | Ukraine, 2012      |
| - Global Supply Chains and GMP Compliance               | Canada, 2013       |

# Future PIC/S Seminar

- Dedicated Facilities or not?  
France, 2014

# Expert Circles / Working Groups

- ✓ APIs
- ✓ Computerised Systems
- ✓ Human Blood, Tissues and Cells
- ✓ Quality Risk Management
- ✓ Good Distribution Practices

Aim: Develop draft guidance documents  
Training in specialised field

# PIC/S Joint Visits

- Started in 1987
- Around 25 groups of 3 inspectors from 3 countries
- 1 inspection per 6 months per country
- for training purposes
- for uniform GMP interpretation
- for uniform inspection procedures
- for mutual confidence

# Relationship with EMA

- EMA attends PIC/S Committee as a Partner
- PIC/S-EU liaison officer attends Inspectors meetings at EMA as an observer
- A harmonised consultation procedure
- Associated Partnership negotiated in 2007 (renewed in 2010)

## Liaison with other organisations

- ✓ The European Department for the Quality of Medicines (EDQM): Associated Partnership negotiated in 2007 (renewed in 2013),
- ✓ UNICEF: Associated Partnership negotiated in 2008,
- ✓ WHO: Co-operation Arrangement negotiated in May 2009
- ✓ ICH,
- ✓ European Commission (DG Health & Consumers)



# Quality system requirements for pharmaceuticals inspectorates

- Reference document : PI 002-3
- Purpose : adopting a common standard for quality system requirements in order to achieve consistency in inspection standards between National Pharmaceutical Inspectorates and thus to facilitate mutual recognition of those Inspectorates

# Quality system requirements for pharmaceuticals inspectorates

## **Main topics**

- ☐ Quality Improvement and Corrective / Preventive Action
- ☐ Complaints
- ☐ Issue and Withdrawal of Licences and GMP certificates
- ☐ Handling Suspected Quality Defects and Rapid Alert System
- ☐ Liaison with OMCL
- ☐ Sub-Contracting and Assessing

# Quality system requirements for pharmaceuticals inspectorates

## **Main topics**

- ☐ Quality Manual
- ☐ Administrative Structure
- ☐ Organisation and Management
- ☐ Documentation and Change Control
- ☐ Records
- ☐ Inspection Procedures
- ☐ Inspection Resources
- ☐ Internal Audit

# Joint Reassessment programme

## Goals

- ❖ To verify that PIC/S member authorities maintain compliance with the requirements of the Scheme (as described in paragraph 8 of the Scheme [PIC/S 1/95 modified]).
- ❖ To verify the implementation of quality system requirements for pharmaceutical inspectorates.
- ❖ To help maintain consistency among PIC/S member authorities

# Typical PIC/S Inspection of a Medicine Manufacturer

## *Before the inspection:*

- Lead inspector assigned.
- Inspection team selected.
  - Technical specialist sometimes included on team
- Company notified.
  - Company requested to provide Site Master File (SMF)
- Inspection team reviews documentation.
  - SMF, complaints, recalls, testing failures, marketing authorisations.
- Lead inspector prepares inspection plan & sends to company.
- Inspection conducted.

# Typical PIC/S Inspection of a Medicine Manufacturer (cont'd)

## *After the inspection:*

- Caucus of inspection team.
- Interim inspection report prepared (deficiencies only).
- Exit interview with company:
  - Attendance sheet completed.
  - Interim inspection report provided (discussion encouraged).
  - Written response requested within 4 weeks.
- Objective evidence assessed by lead inspector.
- If response judged OK, inspection closed out.
- Final inspection report sent to company
- If response not OK, refer to Independent Committee for appropriate action.

## PIC/S Inspection Report

- Identical to the EU Inspection Report format
- SOP for PIC/S Inspection Report format is available on PIC/S web site (document PI 013-3)
- This format used by PIC/S and EU Inspectorates to prepare GMP inspection reports
- Uniform system of classifying GMP deficiencies
  - “critical”, “major” & “other”

# PIC/S Blueprint

- PIC/S Blueprint adopted by PIC/S Committee in December 2005

## Aim:

- ❖ To review PIC/S' mission & goals in a changing environment.
- ❖ To set a number of objectives and actions for the next 10 years.
- ❖ To raise PIC/S' visibility and explain the benefits of PIC/S membership.
- ❖ To make PIC/S more of a global organisation rather than European focussed.

(PIC/S Blueprint is available at [www.picscheme.org](http://www.picscheme.org))



# Recent Developments

- Accession of Japan's MHLW, PMDA & Prefectures and of Korea's MFDS (July 2014)
- New PIC/S GDP Guide, based on EU GDP Guide (June 2014)
- Revision of PIC/S GMP Guide (Part II of GMP Guide (Q7A), Annex 2 and 14) (March 2014)
- Revision of PIC/S Guide to Good Practices for the Preparation of Medicinal Products in Healthcare Establishments (new Annex 3 on radiopharmaceuticals) (March 2014)
- New PIC/S Organisational Sub-Committee Structure (Jan 2014)
- Accession of United Kingdom's Veterinary Agency VMD (Jan 2014)
- Accession of Chinese Taipei's TFDA and New Zealand's Medsafe (Jan 2013)

# PIC/S Executive Bureau

- Joey Gouws (South Africa / MCC), PIC/S Chairperson;
- Paul Hargreaves (UK / MHRA), PIC/S Deputy Chairman and Chair of the Sub-Committee on Budget, Risk and Audit (SCB);
- Helena Baião (Portugal / INFARMED IP), immediate former Chairperson;
- Boon Meow Hoe (Singapore / HSA), Chair of the Sub-Committee on Training (SCT);
- Andreas Krassnigg (Austria / AGES), Chair of the Sub-Committee on Expert Circles (SCEC);
- Jacques Morénas (France / ANSM), Chair of the Sub-Committee on Strategic Development (SCSD);
- Anne Hayes (Ireland / IMB), Chair of the Sub-Committee on Compliance (SCC);
- Paul Gustafson (Canada / HPFBI), Chair of the Sub-Committee on GM(D)P Harmonisation (SCH);
- Tor Gråberg (Sweden / MPA), Chair of the Sub-Committee on Communication (SC COM).

# PIC/S Contacts

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http://www.picscheme.org/

PIC/S

Pharmaceutical Inspection Co-operation Scheme

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Last update 07 December 2011

PIC/S | Role | Benefits | Members & Partners | Activities | Training | Publications | Accession | Links | News

## Welcome to the PIC/S Website!

The Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (jointly referred to as PIC/S) are two international instruments between countries and pharmaceutical inspection authorities, which provide together an active and constructive co-operation in the field of GMP.

PIC/S' mission is "to lead the international development, implementation and maintenance of harmonised Good Manufacturing Practice (GMP) standards and quality systems of inspectorates in the field of medicinal products."

This is to be achieved by developing and promoting harmonised GMP standards and guidance documents; training competent authorities, in particular inspectors; assessing (and reassessing)

## Training

Expert Circle on Blood & Tissue [Read more](#)

Expert Circle on Computerised Systems [Read more](#)

## All the Publications

Q&A Documents

PIC/S GMP Guide

Site Master Files

Most PIC/S publications can be downloaded for free

## News

REVISED PIC/S SCHEME ENTERED INTO FORCE ON 1 JANUARY 2012

[Read more](#)

PIC/S EVENTS IN CAPE TOWN, SOUTH AFRICA, 6-11 NOVEMBER 2011

[Read more](#)